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~~which~~

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5. A DNA sequence according to claim 4 comprising all of the genes listed therein or an allele, mutation or other variant thereof.

5 6. A DNA sequence according to claim 3 encoding at least part of one or more of the polypeptides set out below, said polypeptide having the amino acid sequence as set out in the appended sequence data or being a variant thereof having the specified activity:

10	<u>peptide</u>	<u>activity</u>
	<i>mon CII</i>	epoxyhydrolase/cyclase
	<i>mon E</i>	S-adenosylmethionine-dependent methyltransferase
	<i>mon T</i>	monensin resistance gene
	<i>mon RII</i>	repressor protein
15	<i>mon AIX</i>	thioesterase
	<i>mon AI</i>	polyketide synthase multienzyme
	<i>mon AII</i>	polyketide synthase multienzyme
	<i>mon AIII</i>	polyketide synthase multienzyme
	<i>mon AIV</i>	polyketide synthase multienzyme
20	<i>mon AV</i>	polyketide synthase multienzyme
	<i>mon AVI</i>	polyketide synthase multienzyme
	<i>mon AVII</i>	polyketide synthase multienzyme
	<i>mon AVIII</i>	polyketide synthase multienzyme
	<i>mon H</i>	regulatory protein
25	<i>mon CI</i>	flavin-dependent epoxidase
	<i>mon BII</i>	carbon-carbon double bond isomerase

mon BI carbon-carbon double bond isomerase
mon D cytochrome P450 hydroxylase
mon RI activator protein
mon AX thioesterase

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7. A DNA sequence according to claim 6 encoding a single enzyme activity of a multienzyme encoded by any of *mon AI-mon AVIII* or a variant or part thereof.

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8. A DNA sequence according to any preceding claim encoding any one or more of the domains as set out in Table I or a variant or part thereof.

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9. A DNA sequence according to any preceding claim which has a length of at least 30, preferably at least 60, bases.

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10. A recombinant cloning or expression vector comprising a DNA sequence according to any preceding claim.

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11. A transformant host cell which has been transformed to contain a DNA sequence according to any of claims 1-9 and which is capable of expressing a corresponding polypeptide.

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cont.

12. A hybridisation probe which is a DNA sequence according to any of claims 1-9.

5 13. Use of a probe according to claim 12 to detect a PKS cluster, optionally followed by isolation of the detected cluster.

10 14. Use of a probe according to claim 12 which encodes at least part of a polypeptide having a known function to detect genes encoding polypeptides having analogous function.

15 15. Use according to claim 14 wherein the polypeptide of known function is AT of module 5 or the regulatory protein encoded by *mon RI*.

20 16. A hybridization probe comprising a polynucleotide which binds specifically to a region of the monensin gene cluster selected from *mon BI*, *mon BII*, *mon CI*, *mon CII*, *mon H*, *mon RI*, *mon RII*, *mon T*, *mon AIX* and *mon AX*.

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25 17. Use of a probe according to claim 16 in a method of detecting the presence of a gene cluster which governs the synthesis of a polyether, and optionally isolating a gene cluster detected thereby.

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18. Use of a probe according to claim 12 which comprise a polynucleotide which binds specifically to a gene responsible for levels of activity of the monensin gene cluster, in a method of detecting an analogous gene in a gene cluster for biosynthesis of another polyketide, optionally followed by a step of manipulating the gene detected thereby to alter the level of expression of said other polyketide.

19. Use according to claim 18 wherein the gene is a regulatory gene, resistance gene or thioesterase gene.

20. Use of the *mon RI* gene or variant and a monensin promoter to control expression of a heterologous gene in *S. cinnamonensis*.

21. Use of a portion of the monensin gene cluster encoding a polypeptide having chain terminating activity, preferably comprising at least one of *mon AIX* and *mon AX* or a mutant, allele or other variant thereof encoding a polypeptide having chain terminating activity, to effect chain release of a peptide other than monensin.

22. Use of a portion of the monensin gene cluster encoding a polypeptide having carbon-carbon double bond isomerase activity, preferably comprising at least one of

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mon BI and *mon BII* or a mutant, allele or other variant thereof having isomerase activity to provide a desired stereochemical outcome in the synthesis of a polyketide other than monensin.

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23. A polypeptide encoded by a portion of the monensin gene cluster, preferably comprising at least one of *mon BI* and *mon BII* or a mutant, allele or other variant thereof, having carbon-carbon double bond isomerase activity, or at least one of *mon AIX* and *mon AX* or a mutant, allele or other variant thereof having chain terminating activity.

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24. An epoxidase enzyme encoded by *mon CI* or a derivative or variant thereof having epoxidase activity.

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25. A cyclase enzyme encoded by *mon CII* or a derivative or variant thereof having cyclase activity.

26. Use of a portion of the monensin gene cluster encoding a peptide having epoxidase or cyclase activity, preferably comprising *mon CI* or *mon CII* or a mutant, allele or other variant thereof encoding a polypeptide having epoxidase or cyclase activity to provide a said activity in the biosynthesis of a polypeptide other than monensin.

27. A process for producing a polyketide containing
a desired starter unit comprising providing a PKS gene
having a loading module and a plurality of extension
modules, wherein the loading module includes a KS_q domain
5 derived from a KS domain of a monensin extension module.

28. A process according to claim 27 wherein the KS_q
domain is derived from KS of module 5 of monensin.

10 sub A57 29. A process according to claim 27 or claim 28
wherein the starter unit also includes an AT_q domain
derived from an AT domain which is naturally associated
with the KS domain.

15 30. A DNA sequence comprising DNA encoding at least
one PKS loading module and a plurality of PKS extension
modules, and which can be expressed to produce a
polyketide; wherein at least one of said modules or at
least one domain thereof is a monensin module or domain or
20 a variant thereof and is contiguous to a further one of
said modules or a domain to which it is not naturally
contiguous; provided that the sequence is not an ery
loading module, the first and second extension modules of
the ery PKS and the ery chain-terminating thioesterase in
25 which the DNA encoding AT of the first extension module
has been substituted by DNA encoding an ethyl malonyl-CoA

AT from the monensin gene cluster.

31. A DNA sequence according to claim 30 wherein
said further module or domain is also a monensin module or
5 domain or variant thereof.

32. A DNA sequence according to claim 30 wherein
said further module or domain is a module or domain of a
PKS of a polyketide other than monensin or a variant
10 thereof.

~~sub A67~~ 33. ~~A~~ A DNA sequence according to claim 30, 31 or 32
wherein said ~~loading~~ module is adapted to load a starter
unit other than a starter unit normally received by the
15 adjacent extension module.

34. A DNA sequence according to claim 33 wherein
said loading module is derived from a monensin extension
module or variant thereof.

20 ~~sub A77~~ 35. ~~A~~ A polyketide synthase encoded by the DNA
sequence of any of claims 30-34.

36. A polyketide compound as produced by a synthase
25 according to claim 35.

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37. A vector containing a DNA sequence of any of claims 30-34

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38. A transformant cell transformed to contain a DNA sequence of any of claims 30-34.

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39. A method of producing *S. cinnamonensis* capable of enhanced levels of production of monensin comprising engineering it to overexpress the *mon RI* gene.

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40. A method according to claim 39 wherein said engineering comprises introducing at least one additional copy of the *mon RI* gene as shown in the appended sequence data or a variant thereof.

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41. *S. cinnamonensis* containing multiple copies of the *mon RI* gene as shown in the appended sequence data and/or variant(s) thereof.

42. A method of producing monensin comprising culturing the organism of claim 41 and/or an organism produced by the method of claim 39 or claim 40.

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43. A process for expressing a gene heterologous to *S. cinnamonensis* comprising transforming *S. cinnamonensis* with DNA encoding a heterologous gene and expressing said

gene under control of the activator gene *mon RI* or
actII/orf4.

44. A process according to claim 43 wherein said
5 heterologous gene is a PKS gene.

45. 13-Propyl erythromycin A.

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